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Variance estimation for population attributable risk in a complex cross-sectional animal health survey

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Abstract

Population attributable risk estimates offer a method of combining information on population exposure and disease risk factors into a single measure. Univariate and multivariable methods exist for calculating point estimates and variances under the assumption of equal sampling probabilities. National Animal Health Monitoring System national studies typically use a complex survey design (where selection probabilities vary by design strata), which makes use of these methods of calculating variance inappropriate. We suggest the use of a method called "delete-a-group" jackknife to estimate the variance of population attributable risk when a complex survey design has been implemented. We demonstrate the method using an example of Johne's disease. Advantages of the "delete-a-group" jackknife method include simplicity of implementation and flexibility to estimate variance for any point estimate of interest. Published by Elsevier Science B.V.

Keywords: Population attributable risk; Variance; Estimation; Johne's disease; National Animal Health Monitoring System

1. Introduction

The population attributable risk (PAR), also referred to as "etiologic fraction", "attributable fraction" and "attributable risk" (Kleinbaum et al., 1982) is a useful tool for combining information concerning both the population exposure distribution and the

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effects of single or multiple factors on an individual's disease risk (Walter, 1980). Many definitions have been proposed for PAR. In the case of a single dependent variable, PAR can be defined as the fraction of the overall rate of occurrence of the outcome that can be attributed uniquely to the presence of the risk factor. In a multivariable context, PAR can be defined as the reduction in the proportion of the total disease experience in the population that would be achieved by eliminating the exposure(s) of interest from the population (while distributions of other factors in the population remain unchanged) (Bruzzi et al., 1985; Rockhill et al., 1998).

PAR is widely used by epidemiologists studying diseases in humans in a variety of settings including infectious diseases (Sun et al., 1999; Valeur-Jensen et al., 1999), occupational and environmental epidemiology (Alavanja et al., 1996; Aronson et al., 1996; Loomis et al., 1997) as well as injuries, cancer and other noninfectious diseases (Madigan et al., 1995; Sosin et al., 1996; Perneger et al., 1999). In contrast, use of PAR has not been applied widely in the realm of veterinary epidemiology. Thomas et al. (1981) used PAR in a case-control study of mastitis caused by Mycoplasma species in California dairy herds. Kapperud et al. (1993) estimated the PAR for hygiene and husbandry practices related to the introduction of *Campylobacter* spp into broiler-chicken flocks. Rohrbach et al. (1995) used PAR to determine the risk of laminitis in horses due to exposure to endophyte. Wells et al. (1996), Smith et al. (1998) and Kabagambe et al. (2000) applied PAR to dairy health problems.

Other measures of risk such as odds ratios or relative risks have been more-widely used in veterinary epidemiology — probably (at least in part) due to the widespread knowledge of these estimates. Also, computer software designed to handle the computation of point estimates and associated measures of variability (variance, standard error, confidence intervals) has made these tools readily available for both univariate and multivariable analysis.

An example using PAR in a univariate context will help to demonstrate both the computation as well as the interpretation. Suppose that we are interested in the attributable risk (r_a) for a specific exposure, A, on a disease outcome. The components necessary to compute a univariate PAR include the probability of exposure, P(A), and the relative risk for disease for the exposed versus the unexposed individuals (rr). PAR is calculated (Fleiss, 1981) as

$$r_{\rm a} = \frac{P(A)({\rm rr}-1)}{1 + P(A)({\rm rr}-1)}$$

Suppose, for example, a cross-sectional study yielded a probability of exposure, P(A), equal to 0.1 and a relative risk of 2.0. The PAR would be approximately 0.09, i.e. about 9% of the disease outcome could have been prevented if the affects associated with exposure A were eliminated. Now, suppose the probability of exposure, P(A), equals 0.3 but the relative risk remains at 2.0. The PAR would now be about 0.23. Almost one-fourth of the disease outcome would have been prevented if the affects associated with exposure A were eliminated. This example shows the value of incorporating both the exposure probability and the risk estimate in a single measure because, considered alone, the risk estimate would have been constant. Fleiss (1981) also presents a method for calculating the variance associated with the univariate PAR estimate.

Multivariable techniques (including logistic regression) commonly are used to model epidemiologic data. A multivariable PAR has been developed by Bruzzi et al. (1985) that uses estimates from a logistic model to calculate the effects of an exposure variable after the effects of other exposure variables have been removed. Their method for computing multivariable PAR (r_a) incorporates the proportion of cases (p_j) and the relative risk (rr_j) for each level (j levels) of the risk factor(s):

$$r_{\rm a} = 1 - \sum_{j} \frac{p_j}{{\rm rr}_j}$$

This approach to calculate PAR has been used widely in human epidemiology and, recently, by three veterinary epidemiological studies (Wells et al., 1996; Smith et al., 1998; Kabagambe et al., 2000). Bruzzi et al. (1985), however, did not provide a method for computing variance associated with their point estimate of PAR. Point estimates for PAR provide a measure of central tendency for the sample data but do not provide any measure of precision. Without a measure of precision it is difficult to interpret the meaning of the point estimate. A PAR with a small associated confidence interval (based on a relatively small standard error) provides a narrower range in which you might expect the true PAR to lie compared to the same point estimate with a wider confidence interval. For this reason, it is important to develop a method for creating a measure of precision such as the variance or standard error.

Kooperberg and Petitti (1991) used a data-replication method (called "bootstrapping") to estimate standard errors for PAR from an unmatched case-control study where logistic regression was used to estimate relative risk. Bootstrapping is a method for creating variance estimates where replicate samples are created from the original sample using with-replacement sampling. The replicate samples are used to create an estimated variance. Benichou and Gail (1990) derived variance estimates for PAR using the logistic model under various designs for sampling the controls. Taylor-series expansions (also called the "delta method") were used to estimate the PAR variance. As part of the total variance estimate, they also accounted for the covariances between logistic-model parameters and the proportions of cases by estimating them from a Taylor-series expansion on an implicit function for discrete variables and an influence function for continuous risk factors.

The National Animal Health Monitoring System (NAHMS) first estimated PAR as part of the analysis of the Dairy'96 study, but did not compute an associated measure of variability (Wells et al., 1996). The lack of a variance estimate is due to the nature of the sampling design that NAHMS national studies use. The study-design selection is motivated by the primary purpose of NAHMS studies (which is to produce valid national estimates of animal health and management). NAHMS national studies typically utilize a stratified sampling design with unequal selection probabilities within the strata (Dargatz and Hill, 1996). The goal of this sampling design is to allow for selection of the less-common larger farms (which represent a greater proportion of the animals) at a higher rate than the more-common smaller farms where fewer animals reside. If the selection were entirely random, the small farms would comprise a large proportion of the sample and fewer animals would be represented in the sample. The unequal selection probabilities result in the need to weight the sample data during analysis to produce unbiased population estimates (Dargatz and Hill, 1996). The PAR point estimates for the

Dairy'96 study were created using the appropriate weights to create an unbiased estimate (Wells et al., 1996), but the variance estimate developed by Benichou and Gail (1990) and the bootstrap method applied by Kooperberg and Petitti (1991) assume equal selection probabilities and are not appropriate for the weighted NAHMS sample data. In the absence of an appropriate method for obtaining a valid measure of variance, only the point estimate for PAR was presented.

Several specialized statistical software packages are now available that accommodate weighted data from complex surveys. The most-common approach is to use a Taylor-series expansion to approximate the variance. The software packages will provide variance estimates for a number of statistics including means, proportions and logistic models, but not for PAR. Although it is plausible to create a Taylor-series expansion for PAR, the problem is not trivial. Given the lack of available software or a corresponding weighted method for Benichou and Gail (1990), other options must be sought.

Reporting an unweighted PAR and associated variance is an option but can lead to biased point and variance estimates. Lemeshow et al. (1998) found that descriptive measures (including proportions) can be compromised seriously if the sampling design is ignored. Similarly, the variance can be biased (sometimes in unpredictable directions) if the sampling design and weights are ignored. A measure of the change in variation that can occur when using a complex survey design as compared to a simple random design is called the "design effect". The design effect can be defined as the correct variance estimate for the study design divided by the variance estimate that would have been obtained if the sample was considered to be a simple random sample (Dargatz and Hill, 1996). Dargatz and Hill (1996) showed design effects for a NAHMS cow/calf study that ranged from 0.25 to 3.09. Although there are issues related to the computation of the design effect, their example shows that the variance can be severely under- or overestimated within a single study.

Recently, studies with underlying complex sampling designs have used PAR and have sought other solutions to the problem of obtaining associated variance estimates. Madigan et al. (1995) used a Poisson-regression model to calculate the relative-risk component of PAR for data from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. They chose to ignore the variability of the within risk-factor prevalences (equivalent to the numerator in the multivariable PAR equation) because it was considered small compared to the variability of the incidence rates (the denominator in the multivariable PAR equation).

Basu and Landis (1995) explored the use of two logistic models for PAR using weighted data from a complex, cross-sectional sampling design. Their covariate-adjusted PAR estimator is equivalent to that of Bruzzi et al. (1985) without the rare-disease assumption that must be made to estimate relative risk from observed odds ratios. Although Basu and Landis (1995) treated the exposure prevalences (numerator) as random variables due to the cross-sectional nature of their survey design, they chose to make the assumption of simple random sampling and ignored the weights and complex sample design.

These approaches to implementing PAR in the context of complex survey designs have either made some simplifying assumptions or have ignored features of the sampling design. The objectives of this paper are to apply the multivariable PAR in an animal-production context and to demonstrate the application of a type of variance estimation

procedure called the "jackknife" to estimate an appropriate variance measure for PAR. We describe the typical jackknife estimator but we present an alternative modification called the "delete-a-group" (DAG) jackknife method described in detail by Kott (1998). To demonstrate the utility of the jackknife method in adding value to PAF point estimates, we use the example of a risk-factor model for Johne's disease based on a multiple logistic-regression model using data from the NAHMS Dairy'96 study (Wells and Wagner, 2000).

2. Methods

Jackknife estimation is part of a general class of estimation procedures called "resampling methods" that are used for estimating variance (e.g. mean squared error) or bias (Efron, 1982). Resampling methods often are used when it is difficult to estimate variances directly (as is the case with PAR). When implementing the jackknife, the parameter of interest initially is estimated with the complete data set. Then, the parameter estimates are recalculated repeatedly — each time, with a new single observation deleted from the data until all observations have been omitted a single time. The sum of differences between the each individual estimate and the full estimate times a correction factor provides a measure of the variability.

$$\operatorname{Var}_{\operatorname{jack}} = \frac{n-1}{n} \sum_{i=1}^{n} [\hat{\theta}_{(i)} - \hat{\theta}_{(.)}]^{2}$$

where $\hat{\theta}_{(.)}$ is the overall parameter estimate and $\hat{\theta}_{(i)}$ the parameter estimate with the *i*th observation removed.

To demonstrate the use of a jackknife variance estimate we could examine a simple example of estimating the variance of a mean of a sample of five observations (3, 5, 6, 8, 10). The overall mean equals 6.4 (variance = 1.46, standard error = 1.21). The five replicate means (means calculated with each observation sequentially deleted) are 7.25, 6.75, 6.50, 6.00 and 5.50, respectively. The sum of the squared differences between these means and the overall mean is 1.825. Multiplying the 1.825 by $\frac{4}{5}$ (the coefficient above, (n-1)/n) provides an estimate of the variance of 1.46 and a standard error (square root of the variance of the mean) of 1.21. The parametric equivalent, or the usual variance and standard error, for the full sample is equivalent to the jackknife variance estimate because all samples had the same weights.

Rao et al. (1992) reviewed resampling methods for complex survey designs. They discuss the use of a modified jackknife called the "delete-1-cluster jackknife variance estimator". The delete-1 method is very similar to the simple random-sample equivalent with some modification for the stratification. The weight from the deleted observation is transferred to the remaining observations in the stratum while weights for observations in other strata remain unchanged. SUDAAN¹ (a software package for analyzing complex

¹ SUDAAN: Software for the Statistical Analysis of Correlated Data, Research Triangle Institute, PO Box 12194, Research Triangle Park, NC 27709.

survey data) has adopted this jackknife variance estimator for estimates including means, proportions and logistic regression. Unfortunately, SUDAAN does neither compute PAR nor estimate its associated variance.

Kott (1998) described a version of the jackknife he called the DAG approach. This jackknife deletes a different group of observations per estimate recalculation. Each such recalculation is called a "replicate", which is standard jackknife nomenclature. The DAG jackknife is being used for statistics computed from National Agricultural Statistics Service (NASS) surveys. We chose to use the DAG jackknife method to estimate the variance of PAR. We followed the approach taken by Kott (1998) to implement the DAG jackknife.

The formation of replicate weights (i.e. weights used for the calculation of each jackknife replicate) is the first step in the DAG jackknife estimation process. Kott's instructions are to order the sample so that primary sampling units in the same design stratum are listed together. The design strata are the strata or divisions that are used to facilitate sample selection at the study initiation. The complete sample is then systematically separated into R groups, which are used to create R sets of replicate weights as described below. There are 15 such groups in NASS surveys and we have used the same number for this NAHMS survey. These groups are sequentially "deleted" to form replicate estimates. Operationally, for the rth replicate estimate (r = 1, ..., 15), the weights for each unit in group r are set to zero. Setting the weight of a group to 0 has the affect of removing the observations that comprise the group (approximately $\frac{1}{15}$ of all the observations) from the PAF replicate calculation. For a stratified random sample, the replicate-r weight for a unit not in group r is the unit's weight scaled so that the sum of the replicate weights in a variance stratum equals the sum of the weights prior to deletion of a replicate group. When the weights within stratum are homogeneous, the scaling factor equals the number of observations in the group divided by the number of observations in the group minus 1. The sum of the scaled weights also is the stratum's population size.

Kott (1998) argued that the DAG jackknife can have an unreasonably large bias when the stratum sample size is <5. The NAHMS herd-level data were stratified initially by size class within state. The original design strata were four herd-size classes within 20 states. The number of observations per state/herd-size strata remained above 5 except in the small-herd categories. To assure that there were at least five sample units (herds) in every stratum, state design strata within the same size class were collapsed into regional variance strata. The two smallest herd-size classes (1–49 and 50–99) within the same region likewise were collapsed into each other. This type of collapsing will lead to variance estimates that are, if anything, conservative (Wolter, 1985). The resulting observations in variance strata may have had different sampling fractions and, consequently, weights. Simple scaling of replicate weights will no longer ensure that the sum of the replicate weights will equal the sum of the original stratum weights. Instead, the weights of the remaining observations were scaled by the sum of all the

² Midwest (Iowa, Illinois, Indiana, Michigan, Minnesota, Missouri, Ohio, Wisconsin), Northeast (New York, Pennsylvania, Vermont), Southeast (Florida, Kentucky, Tennessee), West (California, Idaho, New Mexico, Oregon, Texas, Washington).

original weights in the stratum divided by the sum of the weights of the remaining observations in the stratum after an observation was deleted. In this manner, the sums of the replicate weights in each variance stratum were scaled to equal the sums of the original weights in each stratum.

Weighted PAR point estimates were computed following Bruzzi et al. (1985) for the complete data set and for each replicate weight set (n = 15) using a program written in SAS (SAS, 1990). The logistic-model component of PAR was reparameterized from the model presented by Wells and Wagner (2000) to set the risk factor level with the lowest odds ratio to be the reference level (as specified by Bruzzi et al., 1985).

The DAG jackknife variance estimator for the weighted PAR is

$$Var_{par} = \frac{15 - 1}{15} \sum_{i=1}^{15} [ar_{(i)} - ar_{(.)}]^2$$

where $ar_{(i)}$ is the PAR for the *i*th weighted replicate and $ar_{(.)}$ the PAR point estimate from the complete data. The square root of the variance (the standard error) was computed and a 95% confidence interval was constructed using a T-distribution with 14 degrees of freedom (the number of replicates minus one).

During repeated calculation of the PAR required for the DAG jackknife variance estimate, repeated estimates of the components of the PAR (including estimates from the multiple logistic-regression model and the proportion of cases at different levels of risk factors) necessarily were calculated. These replicate estimates were used to calculate DAG variance estimates for each PAR. We also calculated variance estimates for the components of PAR using the two methods available in SUDAAN: jackknife (delete-1) and Taylor-series approximation. Calculation of the variance by three methods allowed for examination of the results to look for patterns or inconsistencies in estimates produced by the methods. SUDAAN will not directly estimate PAR (which motivates the use of the DAG jackknife), so there is no comparison for PAR variance between the DAG jackknife and the variance calculations used by SUDAAN.

3. Results

The multiple logistic-regression model developed by Wells and Wagner (2000) identified five risk factors for a dairy herd being positive under their testing criteria (Table 1). The proportion of cases (Johne's-infected herds) at different levels of these risk factors (the first component of PAR) indicated relatively high percentages of positive herds in the largest herd-size category (300 or more milk cows) and in the Midwest region. The reparameterized logistic-regression model was calculated (reference level set to the lowest risk category) to obtain the second component of the PAR (Table 1).

For each of the five risk factors, PAR point estimates, associated standard errors, and 95% confidence intervals are presented in Table 2. Region of the country and percent of milk cows not born on the operation had the highest PAR point estimates. Specifically, these results suggest that eliminating the effects associated with percent of milk cows not

Table 1
Point estimates for proportion of all positive herds within factors and the reparameterized logistic-model coefficients

| Risk factor and level | No. of responses | Percent of responses | Percent of cases | Betas |
|----------------------------|---------------------------|----------------------|------------------|-------|
| No. of milk cows | | | | |
| Fewer than 100 | 150 | 15.6 | 8.3 | 0.0 |
| 100-299 | 303 | 31.6 | 21.1 | 0.4 |
| 300 or more | 507 | 52.8 | 70.6 | 1.4 |
| Region of the country | | | | |
| West | 220 | 22.9 | 3.7 | 0.0 |
| Midwest | 436 | 45.4 | 66.9 | 0.8 |
| Northeast | 268 | 27.9 | 20.1 | 0.3 |
| Southeast | 36 | 3.8 | 9.3 | 0.2 |
| Percent of milk cows not l | porn on the operation | | | |
| 0% | 267 | 27.8 | 25.4 | 0.0 |
| 1-24% | 379 | 39.5 | 41.5 | 0.5 |
| 25% or more | 314 | 32.7 | 33.1 | 0.7 |
| Use of multiple cow mater | rnity housing in previous | vear | | |
| No | 814 | 84.8 | 42.8 | 0.0 |
| Yes | 146 | 15.2 | 57.2 | 0.4 |
| Use of multiple calf prewe | caned housing in previous | year | | |
| No | 537 | 55.9 | 49.8 | 0.0 |
| Yes | 423 | 44.1 | 50.2 | 0.4 |

born on the operation would prevent almost one-third (33%) of the Johne's-infected herds. Standard errors for the PAR are relatively large with coefficients of variation ranging from 32.5 to 42.0%. The resulting confidence intervals are correspondingly wide and the upper limits are very high for region and percent of milk cows not born on the operation (0.73 and 0.62, respectively).

SUDAAN does not produce a standard-error estimate for the PAR, so there is no available basis for comparing our DAG jackknife standard errors with the standard

Table 2
PAR point estimates with DAG jackknife variance estimates

| Risk factor | PAR point estimate | Standard error | Coefficient of variation | Lower CI | Upper CI |
|---|--------------------|-------------------|--------------------------|-------------|-------------|
| No. of milk cows | 0.14 | 0.05 | 36.64 | 0.03 | 0.24 |
| Region of country | 0.43 | 0.14 | 32.50 | 0.13 | 0.73 |
| Percent of milk cows not born on the operation | 0.33 | 0.14 | 41.60 | 0.04 | 0.62 |
| Use of multiple cow maternity housing in the previous year | 0.15 | 0.06 | 42.00 | 0.01 | 0.28 |
| Use of multiple calf preweaned housing in the previous year | 0.17 | 0.06 | 35.69 | 0.04 | 0.30 |

Table 3 Standard-error estimates for proportion of cases component of PAR

| Risk factor and level | DAG jackknife S.E. | Delete-1 jackknife S.E. | Taylor-series S.E. |
|-----------------------------|-------------------------------|-------------------------|--------------------|
| No. of milk cows | | | |
| Fewer than 100 | 1.0 | 1.3 | 1.3 |
| 100-299 | 2.9 | 3.1 | 2.7 |
| 300 or more | 3.3 | 3.4 | 3.1 |
| Region of the country | | | |
| West | 1.6 | 2.0 | 0.8 |
| Midwest | 4.0 | 3.6 | 3.3 |
| Northeast | 3.5 | 3.1 | 3.0 |
| Southeast | 1.4 | 1.3 | 1.3 |
| Percent of milk cows not b | orn on the operation | | |
| 0% | 5.1 | 3.9 | 3.8 |
| 1-24% | 4.2 | 4.5 | 4.4 |
| 25% or more | 3.9 | 4.1 | 3.9 |
| Use of multiple cow materi | nity housing in previous year | | |
| Yes | 6.0 | 4.5 | 4.4 |
| Use of multiple calf prewed | aned housing in previous year | | |
| Yes | 4.1 | 4.5 | 4.3 |

Table 4 Standard-error estimates for logistic-model coefficients component of PAR

| Parameter | DAG jackknife S.E. | Delete-1 jackknife S.E. | Taylor-series S.E. |
|--------------------------|----------------------------------|-------------------------|--------------------|
| No. of milk cows | | | |
| Fewer than 100 | _ | _ | _ |
| 100-299 | 0.25 | 0.23 | 0.21 |
| 300 or more | 0.28 | 0.31 | 0.30 |
| Region of country | | | |
| West | _ | _ | _ |
| Midwest | 0.31 | 0.28 | 0.28 |
| Northeast | 0.28 | 0.32 | 0.31 |
| Southeast | 0.68 | 0.75 | 0.36 |
| Percent of milk cows no | t born on the operation | | |
| 0% | | _ | _ |
| 1-24% | 0.31 | 0.27 | 0.26 |
| 25% or more | 0.29 | 0.27 | 0.26 |
| Use of multiple cow ma | ternity housing in previous year | | |
| No | _ | _ | _ |
| Yes | 0.28 | 0.22 | 0.21 |
| Use of multiple calf pre | weaned housing in previous year | | |
| No | _ | _ | _ |
| Yes | 0.16 | 0.22 | 0.21 |

errors calculated using the two methods implemented in SUDAAN. However, SUDAAN does produce standard-error estimates for proportions and logistic-model coefficients. DAG standard-error estimates associated with the percent of cases in each risk factor level are similar to those produced using either SUDAAN's Taylor-series approximation and its delete-1 jackknife estimation procedure (Table 3). The DAG standard-error estimates for the logistic-model-coefficients component of PAR tend to be similar to both the Taylor series and jackknife (Table 4). In the southeast region (where the sample size was lowest), both of the jackknife techniques (DAG and SUDAAN) provided standard-error estimates that appeared larger than those from the Taylor-series approximation.

4. Discussion

The DAG methodology provided a straightforward method for calculation of standard errors and confidence intervals under this complex cross-sectional design. Both the study design and the weights were accounted for in the methodology. However, the DAG jackknife assumes at least five observations per stratum, which was not the case in some of our design strata. Prior to performing the DAG jackknife, we collapsed design strata with fewer than five observations into variance stratum. The resulting observations in variance strata had different sampling fractions and, consequently, weights. During the implementation of the DAG jackknife, the weight of the omitted observation is shared with the remaining observations in the stratum. We accounted for the unequal weights by multiplying the weights of the observations remaining in the strata by the ratio of the sum of the original weights and the sum of the weights of the remaining observations. In this manner, the sums of the replicate weights in a variance stratum are scaled to equal the sums of the original weights in each stratum. Biologically, this implies that the management practices and other characteristics of the omitted operation can be represented by the remaining operations in the stratum. Whenever weights are redistributed within any design or post strata (including weights for nonresponse adjustments), there is the potential for introducing some bias but we believe that the regional variance strata that we constructed reflect geographic areas of similar production management.

The DAG estimates of variance were close to but often smaller (11 of 21 estimates) than the variance estimates produced using the jackknife methodology implemented by SUDAAN (delete-1) and larger than the estimates produced using the Taylor-series approximation (15 of 21 estimates). Both jackknife methods appeared to have inflated estimates of variance associated with the logistic-model coefficient for the southeast region relative to the Taylor-series approximation. Compared to the delete-1 method, the DAG method is less computer-intensive (requiring only 15 jackknife iterations versus a number equivalent to the sample size).

PAR allows for the combination of factor-prevalence information and risk-factor models and thus can provide more information than either component alone. Implying outcomes of interest are attributable to specific factors must be done cautiously, however — especially in a study that was undertaken using a cross-sectional design. Rockhill et al.

(1998) listed the assumptions that are necessary to make valid interpretation of the PAR. These assumptions include a causal relationship between the risk factor and the outcome, an immediate reduction in risk by the formerly exposed after the risk factor is eliminated, and independence of the considered risk factors from other factors that may influence disease risk. In this study, two risk factors (region and herd size) likely are surrogates for other risk factors that may include climate, density, and management practices that were not investigated but which relate to the two risk factors. A direct causal mechanism is neither plausible nor do we expect that region and herd size are independent of other unmeasured risk factors. The large associated PAR values, though, suggest that there is a substantial amount of the risk for being positive for Johne's disease that we cannot specifically associate with management factors.

In the context of a cross-sectional study alone, it is not possible to establish the existence of a causal relationship. Examination of relationships that may represent a biological process with causal links is appropriate. In this study, the risk factor with the highest point estimate for PAR (other than region) was the percent of cows not born on the operation. The primary known method of transmission of Johne's disease from herd to herd is through the introduction of infected though healthy-appearing cattle (Sweeney, 1996). The other risk factors that contributed to the PAR both related to multiple-animal housing (maternity cow and preweaning calf). Within-herd transmission is thought to occur most commonly at the time of calving or soon after birth through oral ingestion of infected feces. The risk of transmission may increase if multiple cattle are housed together, resulting in greater exposure of calves to contaminated fecal material.

This study provides the first PAR point and variance (standard errors) estimates for factors in the prevention and control of Johne's disease. The value in calculation of the variance estimates resides in our ability to examine the reliability of these point estimates. Large coefficients of variation and wide confidence intervals should lead to more-conservative inferential conclusions than would result from only assessing the point estimate. Similarly, the variability is indicative of issues that might be considered in designing further studies. These inferences and conclusions are possible due to the implementation of the DAG group method to calculate an appropriate measure of variability for the data obtained from a complex sampling design.

In conclusion, we believe the DAG jackknife method — as a tool for estimating variances under complex survey designs — has two primary advantages. First, the DAG jackknife can be used to estimate the variance for any point estimate of interest in a complex survey without requiring the potentially rigorous process of developing a Taylor-series approximation for the variance. Secondly, implementation of the method is relatively simple and less computer-intensive than a delete-1 jackknife — while providing roughly equivalent variance estimates.

References

Alavanja, M.C.R., Brownson, R.C., Benichou, J., Boice, J., 1996. Estimating the attributable risk of residential radon among nonsmoking women: initial results and methodologic challenges. Environ. Int. 22, S1005– S1013.

- Aronson, K.J., Siemiatycki, J., Dewar, R., Gérin, M., 1996. Occupational risk factors for prostate cancer: results from a case-control study in Montréal, Québec, Canada. Am. J. Epidemiol. 143, 363–373.
- Basu, S., Landis, J.R., 1995. Model-based estimation of population attributable risk under cross-sectional sampling. Am. J. Epidemiol. 142, 1338–1343.
- Benichou, J., Gail, M.H., 1990. Variance calculations and confidence intervals for estimates of the attributable risk based on logistic models. Biometrics 46, 991–1003.
- Bruzzi, P., Green, S.B., Byar, D.P., Brinton, L.A., Schairer, C., 1985. Estimating the population attributable risk for multiple risk factors using case-control data. Am. J. Epidemiol. 122, 904–914.
- Dargatz, D.A., Hill, G.W., 1996. Analysis of survey data. Prev. Vet. Med. 28, 225-237.
- Efron, B., 1982. The jackknife, the bootstrap, and other resampling plans. CBMS-NSF Reg. Conf. Series App. Math., Monograph 38. Soc. Ind. App. Math. Philadelphia, Pennsylvania, 92 pp.
- Fleiss, J.L., 1981. Statistical Methods for Rates and Proportions, 2nd Edition. Wiley, New York, 321 pp.
- Kabagambe, E.K., Wells, S.J., Garber, L.P., Salman, M.D., Wagner, B., Fedorka-Cray, P.J., 2000. Risk factors for fecal shedding of Salmonella in 91 US dairy herds in 1996. Prev. Vet. Med. 43, 177–194.
- Kapperud, G., Skjerve, E., Vik, L., Hauge, K., Lysaker, A., Aalmen, I., Ostroff, S.M., Potter, M., 1993. Epidemiological investigation of risk factors for campylobacter colonization in Norwegian broiler flocks. Epidemiol. Infect. 111, 245–255.
- Kleinbaum, D.G., Kupper, L.L., Morgenstern, H., 1982. Epidemiologic Research: Principles and Quantitative Methods. Van Nostrand Reinhold, New York, 529 pp.
- Kooperberg, C., Petitti, D.B., 1991. Using logistic regression to estimate the adjusted attributable risk of low birthweight in an unmatched case-control study. Epidemiology 2, 363–366.
- Kott, P.S., 1998. Using the delete-a-group jackknife variance estimator in NASS surveys. National Agricultural Statistics Service, Washington, DC, 33 pp.
- Lemeshow, S., Letenneur, L., Dartigues, J.F., Lafont, S., Orgogozo, J., Commenges, D., 1998. Illustration of analysis taking into account complex survey considerations: the association between wine consumption and dementia in the PAQUID study. Am. J. Epidemiol. 148, 298–306.
- Loomis, D.P., Richardson, D.B., Wolf, S.H., Runyan, C.W., Butts, J.D., 1997. Fatal occupational injuries in a southern state. Am. J. Epidemiol. 145, 1089–1099.
- Madigan, M.P., Ziegler, R.G., Benichou, J., Byrne, C., Hoover, R.N., 1995. Proportion of breast cancer cases in the United States explained by well-established risk factors. J. Natl. Cancer Inst. 87, 1681–1685.
- Perneger, T.V., Whelton, P.K., Puddey, I.B., Klag, M.J., 1999. Risk of end-stage renal disease associated with alcohol consumption. Am. J. Epidemiol. 150, 1275–1281.
- Rao, J.N.K., Wu, C.F.J., Yue, K., 1992. Some recent work on resampling methods for complex surveys. Survey Methodol. 18, 209–217.
- Rockhill, B., Newman, B., Weinberg, C., 1998. Use and misuse of population attributable fractions. Am. J. Public Health 88, 15–19.
- Rohrbach, B.W., Green, E.M., Oliver, J.W., Schneider, J.F., 1995. Aggregate risk study of exposure to endophyte-infected (*Acremonium coenophialum*) tall fescue as a risk factor for laminitis in horses. Am. J. Vet. Res. 56, 22–26.
- SAS Institute, 1990. SAS Language: Reference, Version 6, 1st Edition. SAS Institute, Inc., Cary, NC.
- Smith, D.R., Fedorka-Cray, P.J., Mohan, R., Brock, K.V., Wittum, T.E., Morley, P.S., Hoblet, K.H., Saif, L.J., 1998. Epidemiologic herd-level assessment of causative agents and risk factors for winter dysentery in dairy cattle. Am. J. Vet. Res. 59, 994–1001.
- Sosin, D.M., Sacks, J.J., Webb, K.W., 1996. Pediatric head injuries and deaths from bicycling in the United States. Pediatrics 98, 868–870.
- Sun, C., Chen, H., Lu, C., You, S., Mau, Y., Ho, M., Lin, S., Chen, C., 1999. Transmission of hepatitis C virus in Taiwan: prevalence and risk factors based on a nationwide survey. J. Med. Virol. 59, 290–296.
- Sweeney, R.S., 1996. Transmission of paratuberculosis. Paratuberculosis (Johne's disease), Vol. 12. Veterinary Clinics of North America, Food Animal Practice, pp. 305–312.
- Thomas, C.B., Willeberg, P., Jasper, D.E., 1981. Case-control study of bovine mycoplasmal mastitis in California. Am. J. Vet. Res. 42, 511–515.
- Valeur-Jensen, A.K., Pedersen, C.B., Westergaard, T., Jensen, I.P., Lebech, M., Andersen, P.K., Aaby, P.,

Pedersen, B.N., Melbye, M., 1999. Risk factors for parvovirus B19 infection in pregnancy. J. Am. Med. Assoc. 281, 1099–1105.

Walter, S.D., 1980. Prevention for multifactorial diseases. Am. J. Epidemiol. 112, 409-416.

Wells, S.J., Wagner, B.A., 2000. Herd-level risk factors for infection with *Mycobacterium paratuberculosis* in US dairies and association between familiarity of the herd manager with the disease or prior diagnosis of the disease in that herd and use of preventive measures. J. Am. Vet. Med. Assoc. 216 (9), 1450–1457.

Wells, S.J., Dargatz, D.A., Ott, S.L., 1996. Factors associated with mortality to 21 days of life in dairy heifers in the United States. Prev. Vet. Med. 29, 9–19.

Wolter, K.M., 1985. Introduction to Variance Estimation. Springer-Verlag, New York.